Appl. No.: 10/750,076
Amdt. dated February 5, 2007
Reply to Office Action of October 5, 2006

Amendments to the Claims:

1. (Original) A method for preparing an injectable formulation of interferon-beta (IFN-β) comprising:

a) preparing a first solution comprising IFN-β, isolating a pool of purified IFN-β from this solution, and precipitating said IFN-β from this pool using an alcohol to form a precipitate;

b) dissolving said precipitate in guanidine hydrochloride (HCl) to form a second solution comprising resolubilized denatured IFN-β and guanidine HCl;

c) diluting said second solution into a first buffer to obtain a third solution comprising resolubilized renatured IFN-beta and residual guanidine HCl; and

d) removing residual guanidine HCl from said third solution by diafiltration or dialysis of said third solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN-β is prepared.

2. (Original) The method of claim 1, wherein said second buffer contains arginine or sodium chloride.

3. (Original) The method of claim 1, wherein said first buffer has a pH of about 5.0 to about 8.0, and wherein said residual guanidine HCl is present in said third solution at a concentration of 1.6 M or less.

4. (Original) The method of claim 1, wherein said IFN-β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

5. (Currently Amended) The method of claim 1, wherein said IFN-β is glycosylated ~~or unglycosylated~~.

6. (Original) The method of claim 1, wherein said IFN-β is recombinantly produced.

7. (Currently Amended) The method of claim 1, wherein said IFN-β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

8. (Original) A method for preparing an injectable formulation of interferon-beta (IFN-β), said method comprising denaturation of IFN-β with guanidine hydrochloride (HCl) followed by renaturation of the IFN-β via dilution into a first buffer to obtain a renatured IFN-β solution comprising residual guanidine HCl, and removing said residual guanidine HCl from said renatured IFN-β solution by diafiltration or dialysis of said renatured IFN-β solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN-β is prepared.

9. (Original) The method of claim 8, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said renatured IFN-β solution at a concentration of 1.6 M or less.

10. (Original) The method of claim 9, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said renatured IFN-β solution at a concentration of 0.2 M or less.

11. (Original) The method of claim 10, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN-β solution at a concentration of 0.1 M or less.

12. (Original) The method of claim 8, wherein said IFN-β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

13. (Currently Amended) The method of claim 8, wherein said IFN-β is glycosylated ~~or unglycosylated~~.

14. (Original) The method of claim 8, wherein said IFN-β is recombinantly produced.

15. (Currently Amended) The method of claim 8, wherein said IFN-β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

16. (Original) A method for preparing a composition comprising substantially monomeric interferon-beta (IFN-β), said method comprising:

a) preparing a precipitate of substantially purified IFN-β;

b) dissolving said precipitate in guanidine hydrochloride (HCl) to obtain a first solution comprising resolubilized denatured IFN-β; and

c) renaturing said IFN-β by dilution of said first solution with a buffer solution.

17. (Original) The method of claim 16, wherein said buffer solution has a pH of about 5.0 to about 8.0.

18. (Original) The method of claim 16, wherein said IFN-β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

19. (Currently Amended) The method of claim 16, wherein said IFN-β is glycosylated ~~or unglycosylated~~.

20. (Original) The method of claim 16, wherein said IFN-β is recombinantly produced.

21. (Currently Amended) The method of claim 16, wherein said IFN-β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

22. (Original) A method for preparing an injectable formulation of interferon-beta (IFN-β), said method comprising:

a) obtaining a sample comprising substantially purified IFN-β;

b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN-β;

c) diluting said first solution into a first buffer to obtain a second solution comprising solubilized renatured IFN-beta and residual guanidine HCl; and

d) removing residual guanidine HCl from said second solution by diafiltration or dialysis of said second solution into a second buffer that is pharmaceutically acceptable, whereby said injectable formulation of IFN-β is prepared.

23. (Original) The method of claim 22, wherein said first buffer has a pH of about 3.0 to about 5.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 1.6 M or less.

24. (Original) The method of claim 23, wherein said first buffer has a pH of about 3.0 to about 4.0, and wherein said residual guanidine HCl is present in said second solution at a concentration of 0.2 M or less.

25. (Original) The method of claim 24, wherein said first buffer has a pH of about 3.0, and wherein said residual guanidine HCl is present in said renatured IFN-β solution at a concentration of 0.1 M or less.

26. (Original) The method of claim 22, wherein said IFN-β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

27. (Currently Amended) The method of claim 22, wherein said IFN-β is glycosylated ~~or unglycosylated~~.

28. (Original) The method of claim 22, wherein said IFN-β is recombinantly produced.

29. (Currently Amended) The method of claim 22, wherein said IFN-β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.

30. (Original) A method for preparing a composition comprising substantially monomeric interferon-beta (IFN-β), said method comprising:

a) preparing a sample comprising substantially purified IFN-β;

b) mixing said sample with guanidine hydrochloride (HCl) to obtain a first solution comprising solubilized denatured IFN-β; and

c) renaturing said IFN-β by dilution of said first solution with a buffer solution.

31. (Original) The method of claim 30, wherein said buffer solution has a pH of about 3.0 to about 5.0.

32. (Original) The method of claim 30, wherein said IFN-β has the amino acid sequence set forth in SEQ ID NO:1 or SEQ ID NO:2.

33. (Currently Amended) The method of claim 30, wherein said IFN-β is glycosylated ~~or unglycosylated~~.

34. (Original) The method of claim 30, wherein said IFN-β is recombinantly produced.

35. (Currently Amended) The method of claim 30, wherein said IFN-β has at least 80% amino acid sequence identity with the amino acid sequence set forth in SEQ ID NO:1 as calculated using the ALIGN program (version 2.0) with a PAM 120 weight residue table, a gap length penalty of 12, and a gap penalty of 4.